

=> d his

(FILE 'HOME' ENTERED AT 14:08:46 ON 14 SEP 2004)

FILE 'EUROPATFULL, FRFULL, PATDPFULL, PCTFULL, RDISCLOSURE, USPATFULL, USPAT2' ENTERED AT 14:09:13 ON 14 SEP 2004

E TULARIK/PA

L1 316 S E3-E11
L2 24 S L1 AND LXR?
L3 1 S L2 NOT PY>=2000
L4 622 S OXYSTEROL# OR ?EPOXYCHOLESTEROL
L5 578 S L4(L) (HYPERLIPID? OR LDL OR HDL OR LIPID? OR CHOLESTEROL? OR

FILE 'USPATFULL' ENTERED AT 14:16:21 ON 14 SEP 2004

L6 253 S L5
L7 42 S L6 NOT PY>=2000

FILE 'PCTFULL, USPATFULL, USPAT2' ENTERED AT 14:31:23 ON 14 SEP 2004

FILE 'USPATFULL' ENTERED AT 14:31:27 ON 14 SEP 2004

FILE 'REGISTRY' ENTERED AT 15:01:08 ON 14 SEP 2004

E EPOXYCHOLESTEROL/CN
E 24,25-EPOXYCHOLESTEROL/CN

L8 1 S E3

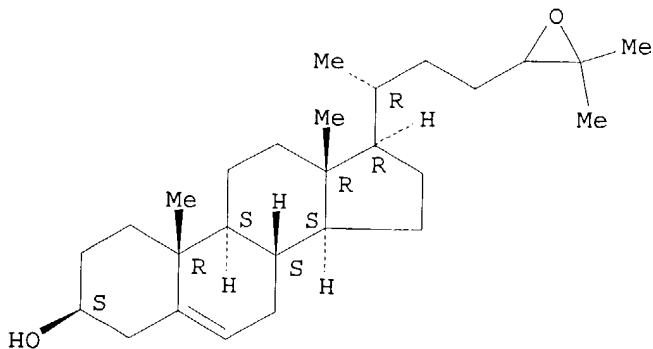
FILE 'CAPLUS' ENTERED AT 15:03:02 ON 14 SEP 2004

L9 26 S L8 OR 24,25-EPOXYCHOLESTEROL
L10 8 S L9(L) (HYPERLIPID? OR LDL OR HDL OR LIPID? OR CHOLESTEROL? OR

=> d rn str cn

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 72542-49-5 REGISTRY

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Cholest-5-en-3-ol, 24,25-epoxy-, (3 β)- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN **24,25-Epoxycholesterol**

CN 24,25-Oxidocholesterol

L2 ANSWER 1 OF 24

ACCESSION NUMBER:
TITLE (ENGLISH):
TITLE (FRENCH):
INVENTOR(S):

PCTFULL COPYRIGHT 2004 Univentio on STN
2003063796 PCTFULL ED 20030818 EW 200332
HETEROCYCLIC ARYLSULFONAMIDOBENZYLIC COMPOUNDS
COMPOSES ARYLSULFONAMIDOBENZYLIQUES HETEROCYCLIQUES
JIAO, Xian, Yun, 1738 South Grant Street, Apt. 5, San
Mateo, CA 94402, US [CN, US];
KAYSER, Frank, 4150 17th Street, #25, San Francisco, CA
94114, US [DE, US];
KOPECKY, David, J., 788 Harrison Street, Apt. #507, San
Francisco, CA 94107, US [US, US];
PIPER, Derek, E., 1226 Church Street, #10, San
Francisco, CA 94114, US [US, US];
SHIAU, Andrew, K., 34 Hugo Street, Apt. 3, San
Francisco, CA 94122, US [US, US];
MCKENDRY, Sharon, 950 Redwood Shores Parkway, Apt.
A105, Redwood City, CA 94065-8482, US [GB, US]

PATENT ASSIGNEE(S):

**TULARIK INC., Two Corporate Drive, South San
Francisco, CA 94080, US [US, US], for all designates
States except US;**
JIAO, Xian, Yun, 1738 South Grant Street, Apt. 5, San
Mateo, CA 94402, US [CN, US], for US only;
KAYSER, Frank, 4150 17th Street, #25, San Francisco, CA
94114, US [DE, US], for US only;
KOPECKY, David, J., 788 Harrison Street, Apt. #507, San
Francisco, CA 94107, US [US, US], for US only;
PIPER, Derek, E., 1226 Church Street, #10, San
Francisco, CA 94114, US [US, US], for US only;
SHIAU, Andrew, K., 34 Hugo Street, Apt. 3, San
Francisco, CA 94122, US [US, US], for US only;
MCKENDRY, Sharon, 950 Redwood Shores Parkway, Apt.
A105, Redwood City, CA 94065-8482, US [GB, US], for US
only

AGENT:

KEZER, William, B.\$, Townsend and Townsend and Crew
LLP, Two Embarcadero Center, 8th Floor, San Francisco,
CA 94111\$, US

LANGUAGE OF FILING:
LANGUAGE OF PUBL.:
DOCUMENT TYPE:
PATENT INFORMATION:

English
English
Patent

NUMBER	KIND	DATE
WO 2003063796	A2	20030807

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG
SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
AM AZ BY KG KZ MD RU TJ TM
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
MC NL PT SE SI SK TR
BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

RW (ARIPO):
RW (EAPO):
RW (EPO):
RW (OAPI):

APPLICATION INFO.:
PRIORITY INFO.:

WO 2003-US3148 A 20030129
US 2002-60/353,496 20020130

L2 ANSWER 2 OF 24

ACCESSION NUMBER:
TITLE (ENGLISH):
TITLE (FRENCH):
INVENTOR(S):

PCTFULL COPYRIGHT 2004 Univentio on STN
2003063576 PCTFULL ED 20030818 EW 200332
ARYLSULFONAMIDOBENZYLIC COMPOUNDS
COMPOSES ARYLSULFONAMIDOBENZYLIQUES
JIAO, Xian, Yun, 1738 South Grant Street, Apt. 5, San
Mateo, CA 94402, US [CN, US];
KAYSER, Frank, 4150 17th Street, #25, San Francisco, CA
94114, US [DE, US];
KOPECKY, David, J., 788 Harrison Street, Apt. #507, San
Francisco, CA 94107, US [US, US];
MCKENDRY, Sharon, 231 30th Street, San Francisco, CA

94131, US [GB, US];
PIPER, Derek, E., 1226 Church Street, #10, San Francisco, CA 94114, US [US, US];
SHIAU, Andrew, K., 34 Hugo Street, Apt. 3, San Francisco, CA 94122, US [US, US]

PATENT ASSIGNEE(S) :

TULARIK INC., Two Corporate Drive, South San Francisco, CA 94080, US [US, US], for all designates States except US;

JIAO, Xian, Yun, 1738 South Grant Street, Apt. 5, San Mateo, CA 94402, US [CN, US], for US only;
KAYSER, Frank, 4150 17th Street, #25, San Francisco, CA 94114, US [DE, US], for US only;
KOPECKY, David, J., 788 Harrison Street, Apt. #507, San Francisco, CA 94107, US [US, US], for US only;
MCKENDRY, Sharon, 231 30th Street, San Francisco, CA 94131, US [GB, US], for US only;
PIPER, Derek, E., 1226 Church Street, #10, San Francisco, CA 94114, US [US, US], for US only;
SHIAU, Andrew, K., 34 Hugo Street, Apt. 3, San Francisco, CA 94122, US [US, US], for US only

AGENT :

KEZER, William, B.\$, Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111\$, US

LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003063576	A2	20030807

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG
SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
MC NL PT SE SI SK TR

RW (OAPI):

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2003-US3149 A 20030129

PRIORITY INFO.:

US 2002-60/353,497 20020130

L2 ANSWER 3 OF 24

PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER:

2002081691 PCTFULL ED 20021028 EW 200242

TITLE (ENGLISH):

ABCG5 AND ABCG8: COMPOSITIONS AND METHODS OF USE

TITLE (FRENCH):

ABCG5 ET ABCG8: COMPOSITIONS ET PROCEDES D'UTILISATION

INVENTOR(S):

HOBBS, Helen, H., 5117 Palomar, Dallas, TX 95229, US;
SHAN, Bei, 349 Quay Lane, Redwood City, CA 94065, US;
BARNES, Robert, 8583 Santa Clara, Frisco, TX 75034, US;
TIAN, Hui, 1179 Foster City Blvd., Foster City, CA 94404, US

PATENT ASSIGNEE(S) :

TULARIK INC., Two Corporate Drive, South San Francisco, CA 94080, US [US, US];

BOARD OF REGENTS, UNIVERSITY OF TEXAS SYSTEM, 201 W. 7th Street, Austin, TX 78701, US [US, US]

AGENT :

GARRETT-WACKOWSKI, Eugenia\$, Townsend and Townsend and Crew LLP, Two Embarcadero Center, Eighth Floor, San Francisco, CA 94111\$, US

LANGUAGE OF FILING:

English

LANGUAGE OF PUBL.:

English

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002081691	A2	20021017

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
 CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
 IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
 MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK
 SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
 RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZW
 RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
 RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 TR
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
 APPLICATION INFO.: WO 2001-US43823 A 20011120
 PRIORITY INFO.: US 2000-60/252,235 20001120
 US 2000-60/253,645 20001128

L2 ANSWER 4 OF 24 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2002064125 PCTFULL ED 20020904 EW 200234
 TITLE (ENGLISH): THERAPEUTIC AGENT FOR HYPERLIPIDEMIA
 TITLE (FRENCH): AGENT THERAPEUTIQUE CONTRE L'HYPERLIPIDEMIE
 INVENTOR(S): TOJO, Shinichiro, 7-26-704, Higashiyama-cho,
 Ashiya-shi, Hyogo 659-0091, JP [JP, JP];
 NITA, Masahiro, 2-13-25-703, Nakashinkai,
 Higashiosaka-shi, Osaka 578-0911, JP [JP, JP];
 NISHIMURA, Takeski, c/o Josephine Sederlin,
 Flemmingsberg Lagenhet 130, Terpivagen 10B, 4tr, S-141
 55 Huddinge, SE [SE, SE];
 SHAN, Bei, 349 Quay Lane, Redwood City, CA 94065, US
 [US, US]
 PATENT ASSIGNEE(S): SUMITOMO PHARMACEUTICALS COMPANY, LIMITED, 2-8,
 Doshomachi 2-chome, Chuo-ku, Osaka-shi, Osaka 541-8510,
 JP [JP, JP], for all designates States except US;
**TULARIK INC., Two Coporate Drive, South San
 Francisco, CA 94080, US [US, US], for all designates
 States except US;**
 TOJO, Shinichiro, 7-26-704, Higashiyama-cho,
 Ashiya-shi, Hyogo 659-0091, JP [JP, JP], for US only;
 NITA, Masahiro, 2-13-25-703, Nakashinkai,
 Higashiosaka-shi, Osaka 578-0911, JP [JP, JP], for US
 only;
 NISHIMURA, Takeski, c/o Josephine Sederlin,
 Flemmingsberg Lagenhet 130, Terpivagen 10B, 4tr, S-141
 55 Huddinge, SE [SE, SE], for US only;
 SHAN, Bei, 349 Quay Lane, Redwood City, CA 94065, US
 [US, US], for US only
 AGENT: KILYK, John, Jr. \$, Leydig, Voit & Mayer, Ltd., Suite
 4900, Two Prudential Plaza, 180 North Stetson, Chicago,
 IL 60601-6780\$, US
 LANGUAGE OF FILING: English
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002064125	A2	20020822

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CO CR CU
 CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU IL IN
 IS KE KG KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX
 MZ NO NZ OM PL PT RO RU SD SE SG SI SK SL TJ TM TN TR
 TT TZ UA UG US UZ VN YU ZA ZM ZW
 RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
 RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
 RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 TR
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
 APPLICATION INFO.: WO 2002-US4153 A 20020212
 PRIORITY INFO.: US 2001-09/782,535 20010213

ACCESSION NUMBER: 2002020463 PCTFULL ED 20020705 EW 200211
 TITLE (ENGLISH): FXR MODULATORS
 TITLE (FRENCH): MODULATEURS FXR
 INVENTOR(S): HOUZE, Jonathan, 2383 Ticonderoga Drive, San Mateo, CA 94402, US [US, US];
 MCKENDRY, Sharon, 231 30th Street, San Francisco, CA 94131, US [GB, US];
 GERGELY, Joshua, P., 650 Guerrero Street, San Francisco, CA 94110, US [US, US];
 XIA, Yi, 1631 Marcie Circle, South San Francisco, CA 94080, US [CN, US];
 SHAN, Bei, 349 Quay Lane, Redwood City, CA 94065, US [US, US];
 KAYSER, Frank, 4150 17th Street, Apt. #25, San Francisco, CA 94114, US [DE, US]

PATENT ASSIGNEE(S): **TULARIK INC., Two Corporate Drive, South San Francisco, CA 94080, US [US, US], for all designates States except US;**
 HOUZE, Jonathan, 2383 Ticonderoga Drive, San Mateo, CA 94402, US [US, US], for US only;
 MCKENDRY, Sharon, 231 30th Street, San Francisco, CA 94131, US [GB, US], for US only;
 GERGELY, Joshua, P., 650 Guerrero Street, San Francisco, CA 94110, US [US, US], for US only;
 XIA, Yi, 1631 Marcie Circle, South San Francisco, CA 94080, US [CN, US], for US only;
 SHAN, Bei, 349 Quay Lane, Redwood City, CA 94065, US [US, US], for US only;
 KAYSER, Frank, 4150 17th Street, Apt. #25, San Francisco, CA 94114, US [DE, US], for US only
 AGENT: SNYDER, Joseph, R.\$, Townsend and Townsend and Crew LLP, Two Embarcadero Center, Eighth Floor, San Francisco, CA 94111\$, US

LANGUAGE OF FILING: English
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2002020463	A2	20020314
DESIGNATED STATES	W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW		
RW (ARIPO):	GH GM KE LS MW MZ SD SL SZ TZ UG ZW		
RW (EAPO):	AM AZ BY KG KZ MD RU TJ TM		
RW (EPO):	AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR		
RW (OAPI):	BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 2001-US27239	A	20010831
PRIORITY INFO.:	US 2000-60/230,585		20000905
	US 2000-60/258,092		20001222

L2 ANSWER 6 OF 24 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2001082917 PCTFULL ED 20020826
 TITLE (ENGLISH): TREATMENT OF HYPERTRIGLYCERIDEMIA AND OTHER CONDITIONS USING **LXR** MODULATORS
 TITLE (FRENCH): TRAITEMENT DE L'HYPERTRIGLYCERIDEMIE ET D'AUTRES MALADIES AU MOYEN DE MODULATEURS **LXR**
 INVENTOR(S): SHAN, Bei;
 SCHULTZ, Joshua;
 TU, Hua
 PATENT ASSIGNEE(S): **TULARIK INC.;**
 SHAN, Bei;
 SCHULTZ, Joshua;
 TU, Hua

DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001082917	A2	20011108

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US14586 A 20010503
PRIORITY INFO.: US 2000-60/201,601 20000503

L2 ANSWER 7 OF 24

PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2001079272 PCTFULL ED 20020826

TITLE (ENGLISH): SITOSTEROLEMIA SUSCEPTIBILITY GENE (SSG): COMPOSITIONS
AND METHODS OF USE

TITLE (FRENCH): GENE DE SUSCEPTIBILITE A LA SITOSTEROLEMIE (SSG):
COMPOSITIONS ET METHODES D'UTILISATION

INVENTOR(S): TIAN, Hui;
SCHULTZ, Joshua;
SHAN, Bei

PATENT ASSIGNEE(S): **TULARIK INC.**;
TIAN, Hui;
SCHULTZ, Joshua;
SHAN, Bei

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001079272	A2	20011025

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US12758 A 20010418
PRIORITY INFO.: US 2000-60/198,465 20000418
US 2000-60/204,234 20000515

L2 ANSWER 8 OF 24

PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2001077067 PCTFULL ED 20020822

TITLE (ENGLISH): SOLID PHASE SYNTHESIS OF **LXR** LIGANDS

TITLE (FRENCH): SYNTHESE EN PHASE SOLIDE POUR LIGANDS **LXR**

INVENTOR(S): MEDINA, Julio;
IMAZAKI, Naonori

PATENT ASSIGNEE(S): **TULARIK INC.**;
SUMITOMO PHARMACEUTICALS;
MEDINA, Julio;
IMAZAKI, Naonori

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001077067	A2	20011018

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM

TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US11242 A 20010405
PRIORITY INFO.: US 2000-60/194,911 20000405
US 2001-09/827,837 20010404

L2 ANSWER 9 OF 24 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2001060818 PCTFULL ED 20020822
TITLE (ENGLISH): LXR MODULATORS
TITLE (FRENCH): MODULATEURS LXR
INVENTOR(S): LI, Leping;
MEDINA, Julio, Cesar;
SHAN, Bei
PATENT ASSIGNEE(S): TULARIK INC.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001060818	A1	20010823

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE
DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE
KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX
NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA
UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM
AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB
GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML
MR NE SN TD TG

APPLICATION INFO.: WO 2000-US3806 A 20000214

L2 ANSWER 10 OF 24 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2001003705 PCTFULL ED 20020828
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR RAISING HDL CHOLESTEROL
LEVELS
TITLE (FRENCH): COMPOSITIONS ET METHODES PERMETTANT D'AUGMENTER LES
TAUX DE HDL CHOLESTEROL
INVENTOR(S): SHAN, Bei
PATENT ASSIGNEE(S): TULARIK INC.;
SHAN, Bei
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001003705	A1	20010118

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG
CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US18533 A 20000707
PRIORITY INFO.: US 1999-60/142,994 19990708
US 2000-09/612,135 20000707

L2 ANSWER 11 OF 24 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2000054759 PCTFULL ED 20020515
TITLE (ENGLISH): LXR MODULATORS
TITLE (FRENCH): MODULATEURS DU LXR
INVENTOR(S): LI, Leping;
MEDINA, Julio, C.;
HASEGAWA, Hirohiko;
CUTLER, Serena, T.;
LIU, Jiwen;

PATENT ASSIGNEE(S): ZHU, Liusheng;
LANGUAGE OF PUBL.: SHAN, Bei;
DOCUMENT TYPE: LUSTIG, Kevin
PATENT INFORMATION: **TULARIK INC.**
English
Patent

NUMBER	KIND	DATE
WO 2000054759	A2	20000921

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE
DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW
MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ
UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW
AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR
GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW
ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US6611 A 20000315
PRIORITY INFO.: US 1999-60/124,525 19990315

L2 ANSWER 12 OF 24 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2000040965 PCTFULL ED 20020515

TITLE (ENGLISH): FXR RECEPTOR-MEDIATED MODULATION OF CHOLESTEROL
METABOLISM

TITLE (FRENCH): MODULATION DU METABOLISME DU CHOLESTEROL INDUITE PAR LE
RECEPTEUR FXR

INVENTOR(S): SHAN, Bei;
OKAMOTO, Arthur, Y.

PATENT ASSIGNEE(S): **TULARIK, INC.**
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent

NUMBER	KIND	DATE
WO 2000040965	A1	20000713

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE
DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE
KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX
NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA
UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM
AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB
GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML
MR NE SN TD TG

APPLICATION INFO.: WO 2000-US431 A 20000106
PRIORITY INFO.: US 1999-60/115,249 19990107

L2 ANSWER 13 OF 24 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 1999027365 PCTFULL ED 20020515

TITLE (ENGLISH): NUCLEAR HORMONE RECEPTOR DRUG SCREENS

TITLE (FRENCH): CRIBLES POUR MEDICAMENTS RECEPTEURS DE L'HORMONE
NUCLEAIRE

INVENTOR(S): LUSTIG, Kevin;
BAEUERLE, Patrick;
BECKMANN, Holger;
CHEN, Jin-Long;
SHAN, Bei

PATENT ASSIGNEE(S): **TULARIK INC.**
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent

NUMBER	KIND	DATE
WO 9927365	A1	19990603

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE

ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU
 SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM
 KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE
 CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ
 CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1998-US24969 A 19981120
 PRIORITY INFO.: US 1997-08/975,614 19971121
 US 1998-09/163,713 19980930

L2 ANSWER 14 OF 24 USPATFULL on STN
 ACCESSION NUMBER: 2004:228040 USPATFULL
 TITLE: FXR modulators
 INVENTOR(S): Houze, Jonathan, San Mateo, CA, UNITED STATES
 McKendry, Sharon, San Francisco, CA, UNITED STATES
 Gergely, Joshua P., San Francisco, CA, UNITED STATES
 Xia, Yi, South San Francisco, CA, UNITED STATES
 Shan, Bei, Redwood City, CA, UNITED STATES
 Kayser, Frank, San Francisco, CA, UNITED STATES
 PATENT ASSIGNEE(S): **Tularik, Inc.**, South San Francisco, CA (U.S.
 corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004176426	A1	20040909
APPLICATION INFO.:	US 2004-794228	A1	20040304 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2001-945293, filed on 31 Aug 2001, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-258092P	20001222 (60)
	US 2000-230585P	20000905 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	35	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	15 Drawing Page(s)	
LINE COUNT:	1954	

L2 ANSWER 15 OF 24 USPATFULL on STN
 ACCESSION NUMBER: 2004:196827 USPATFULL
 TITLE: Solid phase synthesis of **LXR** ligands
 INVENTOR(S): Medina, Julio, San Carlos, CA, UNITED STATES
 Imazaki, Naonori, Osaka, JAPAN
 PATENT ASSIGNEE(S): **Tularik Inc.**, So. San Francisco, CA (U.S.
 corporation)
 Sumitomo Pharmaceuticals Co., Ltd., Osaka, JAPAN (U.S.
 corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004152132	A1	20040805
APPLICATION INFO.:	US 2003-749530	A1	20031230 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2001-827837, filed on 4 Apr 2001, GRANTED, Pat. No. US 6673543		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-194911P	20000405 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	22	
EXEMPLARY CLAIM:	1	

NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1136
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 16 OF 24 USPATFULL on STN
ACCESSION NUMBER: 2003:325111 USPATFULL
TITLE: Arylsulfonamidobenzyllic compounds
INVENTOR(S): Jiao, Xian Yun, San Mateo, CA, UNITED STATES
Kayser, Frank, San Francisco, CA, UNITED STATES
McKendry, Sharon, Redwood Shores, CA, UNITED STATES
Piper, Derek E., Foster City, CA, UNITED STATES
Shiau, Andrew K., San Francisco, CA, UNITED STATES
PATENT ASSIGNEE(S): **Tularik Inc.**, So. San Francisco, CA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003229093	A1	20031211
APPLICATION INFO.:	US 2003-354922	A1	20030129 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-353497P	20020130 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	36	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3129	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 17 OF 24 USPATFULL on STN
ACCESSION NUMBER: 2003:312734 USPATFULL
TITLE: Heterocyclic arylsulfonamidobenzyllic compounds
INVENTOR(S): Jiao, Xian Yun, San Mateo, CA, UNITED STATES
Kayser, Frank, San Francisco, CA, UNITED STATES
Kopecky, David J., San Francisco, CA, UNITED STATES
McKendry, Sharon, Redwood Shores, CA, UNITED STATES
Piper, Derek E., Foster City, CA, UNITED STATES
Shiau, Andrew K., San Francisco, CA, UNITED STATES
PATENT ASSIGNEE(S): **Tularik Inc.**, So. San Francisco, CA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003220339	A1	20031127
APPLICATION INFO.:	US 2003-354923	A1	20030129 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-353496P	20020130 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	36	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1971	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 18 OF 24 USPATFULL on STN
ACCESSION NUMBER: 2003:115720 USPATFULL
TITLE: Nuclear hormone receptor fluorescence polarization assay
INVENTOR(S): Lustig, Kevin, South San Francisco, CA, United States
Bauerle, Patrick, South San Francisco, CA, United States

Beckmann, Holger, South San Francisco, CA, United States
Chen, Jin-Long, South San Francisco, CA, United States
Shan, Bei, South San Francisco, CA, United States
Tularik Inc., South San Francisco, CA, United States (U.S. corporation)

PATENT ASSIGNEE(S):

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6555326	B1	20030429
APPLICATION INFO.:	US 1997-975614		19971121 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Pak, Michael		
LEGAL REPRESENTATIVE:	Osman, Richard Aton		
NUMBER OF CLAIMS:	18		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 4 Drawing Page(s)		
LINE COUNT:	454		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 19 OF 24 USPATFULL on STN
ACCESSION NUMBER: 2003:3485 USPATFULL
TITLE: FXR receptor-mediated modulation of cholesterol metabolism
INVENTOR(S): Shan, Bei, Redwood City, CA, UNITED STATES
Okamoto, Arthur Y., San Mateo, CA, UNITED STATES
PATENT ASSIGNEE(S): **Tularik Inc., a Delaware Corporation** (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003003520	A1	20030102
APPLICATION INFO.:	US 2002-217293	A1	20020812 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2000-478948, filed on 6 Jan 2000, GRANTED, Pat. No. US 6465258		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115249P	19990107 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	47	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	14 Drawing Page(s)	
LINE COUNT:	1817	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 20 OF 24 USPATFULL on STN
ACCESSION NUMBER: 2002:268615 USPATFULL
TITLE: FXR receptor-mediated modulation cholesterol metabolism
INVENTOR(S): Shan, Bei, Redwood City, CA, United States
Okamoto, Arthur Y, San Mateo, CA, United States
PATENT ASSIGNEE(S): **Tularik, Inc.**, South San Francisco, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6465258	B1	20021015
APPLICATION INFO.:	US 2000-478948		20000106 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115249P	19990107 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	

PRIMARY EXAMINER: Whisenant, Ethan C.
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP
NUMBER OF CLAIMS: 47
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 1921
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 21 OF 24 USPATFULL on STN
ACCESSION NUMBER: 2002:221992 USPATFULL
TITLE: FXR modulators
INVENTOR(S): Houze, Jonathan, San Mateo, CA, UNITED STATES
McKendry, Sharon, San Francisco, CA, UNITED STATES
Gergely, Joshua P., San Francisco, CA, UNITED STATES
Xia, Yi, South San Francisco, CA, UNITED STATES
Shan, Bei, Redwood City, CA, UNITED STATES
Kayser, Frank, San Francisco, CA, UNITED STATES
PATENT ASSIGNEE(S): **Tularik Inc.**, South San Francisco, CA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002120137	A1	20020829
	US 6777446	B2	20040817
APPLICATION INFO.:	US 2001-945293	A1	20010831 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-258092P	20001222 (60)
	US 2000-230585P	20000905 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Page(s)
LINE COUNT: 1959
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 22 OF 24 USPATFULL on STN
ACCESSION NUMBER: 2001:202683 USPATFULL
TITLE: **LXR** modulators
INVENTOR(S): Li, Leping, Burlingame, CA, United States
Medina, Julio C., San Carlos, CA, United States
Lustig, Kevin, South San Francisco, CA, United States
Shan, Bei, Redwood City, CA, United States
Hasegawa, Hirohiko, Osaka, Japan
Cutler, Serena T., Palo Alto, CA, United States
Liu, Jiwen, Burlingame, CA, United States
Zhu, Liusheng, Burlingame, CA, United States
PATENT ASSIGNEE(S): **Tularik Inc.**, So. San Francisco, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6316503	B1	20011113
APPLICATION INFO.:	US 2000-525861		20000314 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lambkin, Deborah C.
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP
NUMBER OF CLAIMS: 47
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 2631
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 23 OF 24 USPAT2 on STN
ACCESSION NUMBER: 2002:221992 USPAT2
TITLE: FXR modulators
INVENTOR(S): Houze, Jonathan, San Mateo, CA, United States
McKendry, Sharon, San Francisco, CA, United States
Gergely, Joshua P., San Francisco, CA, United States
Xia, Yi, South San Francisco, CA, United States
Shan, Bei, Redwood City, CA, United States
Kayser, Frank, San Francisco, CA, United States
PATENT ASSIGNEE(S): **Tularik, Inc.**, South San Francisco, CA,
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6777446	B2	20040817
APPLICATION INFO.:	US 2001-945293		20010831 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-258092P	20001222 (60)
	US 2000-230585P	20000905 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Raymond, Richard L.
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Figure(s); 15 Drawing Page(s)
LINE COUNT: 1726
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 24 OF 24 USPAT2 on STN
ACCESSION NUMBER: 2002:141091 USPAT2
TITLE: Solid phase synthesis of **LXR** ligands
INVENTOR(S): Medina, Julio, San Carlos, CA, United States
Imazaki, Naonori, Osaka, JAPAN
PATENT ASSIGNEE(S): **Tularik, Inc.**, So. San Francisco, CA, United
States (U.S. corporation)
Sumitomo Pharmaceuticals Co., Ltd., Osaka, JAPAN
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6673543	B2	20040106
APPLICATION INFO.:	US 2001-827837		20010404 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-194911P	20000405 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Celsa, Bennett
ASSISTANT EXAMINER: Epperson, Jon D.
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1009
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1985:2444 CAPLUS
DOCUMENT NUMBER: 102:2444
TITLE: Oxygenated sterols as inhibitors of enzymic conversion
of dihydrolanosterol into cholesterol
AUTHOR(S): Sato, Yoshihiro; Sonoda, Yoshiko; Morisaki, Masuo;
Ikekawa, Nobuo
CORPORATE SOURCE: Kyoritsu Coll. Pharm., Tokyo, 105, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1984), 32(8),
3305-8
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 5 α -Cholest-8(14)-en-3 β -ol-15-one, 7-oxocholesterol,
24-oxocholesterol, (24S)-**24,25-**
epoxycholesterol, (24R)-**24,25-**
epoxycholesterol, (22S)-22-hydroxycholesterol, and
(22R)-22-hydroxycholesterol at 40 μ M inhibited **cholesterol**
biosynthesis from 24,25-dihydrolanosterol by rat liver subcellular 10,000
g supernatant fraction. 5 α -Cholest-8(14)-en-3 β -ol-15-one had
the greatest effect (64% inhibition). The inhibitory effect was highly
dependent on the configuration of the epoxide or the hydroxy on the side
chain: (24S)-**24,25-epoxycholesterol** and
(22R)-22-hydroxycholesterol were more potent inhibitors than the resp.
24R- and 22S isomers. The results also indicate that 3-hydroxy-3-
methylglutaryl-CoA reductase was not the sole target enzyme of sterol
synthesis inhibition by oxygenated sterols, but lanosterol demethylation
and(or) the subsequent transformation leading to **cholesterol**
were also affected.

AB 5 α -Cholest-8(14)-en-3 β -ol-15-one, 7-oxocholesterol,
24-oxocholesterol, (24S)-**24,25-**
epoxycholesterol, (24R)-**24,25-**
epoxycholesterol, (22S)-22-hydroxycholesterol, and
(22R)-22-hydroxycholesterol at 40 μ M inhibited **cholesterol**
biosynthesis from 24,25-dihydrolanosterol by rat liver subcellular 10,000
g supernatant fraction. 5 α -Cholest-8(14)-en-3 β -ol-15-one had
the greatest effect (64% inhibition). The inhibitory effect was highly
dependent on the configuration of the epoxide or the hydroxy on the side
chain: (24S)-**24,25-epoxycholesterol** and
(22R)-22-hydroxycholesterol were more potent inhibitors than the resp.
24R- and 22S isomers. The results also indicate that 3-hydroxy-3-
methylglutaryl-CoA reductase was not the sole target enzyme of sterol
synthesis inhibition by oxygenated sterols, but lanosterol demethylation
and(or) the subsequent transformation leading to **cholesterol**
were also affected.

TITLE: Effects of a 2,3-oxidosqualene-lanosterol cyclase inhibitor, 2,3: 22,23-dioxidosqualene and **24,25-epoxycholesterol** on the regulation of **cholesterol** biosynthesis in human hepatoma cell line HepG2

AUTHOR(S): Dollis, Daniele; Schuber, Francis

CORPORATE SOURCE: Laboratoire Chimie Bioorganique, Faculte Pharmacie, Illkirch, 67400, Fr.

SOURCE: Biochemical Pharmacology (1994), 48(1), 49-57
CODEN: BCPA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB N-[1(1,5,9)-trimethyldecyl]-4 α , 10-dimethyl-8-aza-trans-decal-3 β -ol (8-azadecalin 1), a high-energy intermediate analog for the 2,3-oxidosqualene-lanosterol cyclase, was found to be a powerful (IC₅₀ \approx 0.1 μ M) inhibitor of **cholesterol** biosynthesis in human hepatoma HepG2 cells. In anal. with other mammalian cells grown in the presence of cyclase inhibitors, the decrease in C27-sterol formation was accompanied by an accumulation of 2,3-oxidosqualene, 2,3:22,23-dioxidosqualene, and by the formation of a compound characterized as **24,25-epoxycholesterol**, a repressor of HMG-CoA (3-hydroxy-3-methylglutaryl CoA) reductase activity. In order to assess the cyclase as a potential pharmacol. target for the design of hypocholesterolemic drugs, it is important to test whether inhibitors of this enzyme are able to act synergistically on the biosynthesis of **cholesterol**, i.e. by decreasing the amount of lanosterol formed and by repressing the regulatory HMG-CoA reductase via the formation of regulatory oxysterols. The accumulation of **24,25-epoxycholesterol** in relationship to the decrease of C27-sterol biosynthesis and of HMG-CoA reductase activity showed only a partial correlation: e.g. at [1] = 100 + IC₅₀ only a 50% reduction in enzyme activity could be attained. In contrast, when HepG2 cells were treated with 2,3:22,23-dioxidosqualene or **24,25-epoxycholesterol**, excellent correlations were found between the inhibition of C27-sterol biosynthesis and the repression of HMG-CoA reductase activity, which was almost complete at the highest concns. of these epoxides (10⁻⁵ M). Altogether, the authors' results suggest that treatment of HepG2 cells with a cyclase inhibitor such as 8-azadecalin (1) does not lead to an intracellular accumulation of repressor mols. high enough to fully trigger a regulatory pathway resulting in a complete down-regulation of HMG-CoA reductase. At intermediary concns. of cyclase inhibitors (IC₅₀), however, a synergistic mode of action of these inhibitors seems plausible.

TI Effects of a 2,3-oxidosqualene-lanosterol cyclase inhibitor, 2,3: 22,23-dioxidosqualene and **24,25-epoxycholesterol** on the regulation of **cholesterol** biosynthesis in human hepatoma cell line HepG2